REMARKS

Independent claims 1 and 140 have been amended to further highlight their patentability over the prior art of record. Dependent claims 3 and 4 have also been amended. Claims 5 and 142 were previously canceled, and claims 42-139 previously withdrawn.. Dependent claims 2, 6-41, 141 and 143 remain unchanged. Applicants also present arguments below in further support of the patentability of all claims in view of the rejections set forth in the pending *Final Office Action*.

Claims 1-4, 6-41, 140, 141 And 143 Stand Rejected Under 35 U.S.C. §103(a)

Claims 1-4, 6-40, 140, 141 and 143 stand rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent 6,468,506 to *Rössling et al.* in view of U.S. Patent 6,397,098 to *Uber, III et al.* and, variously, further in view of International Publication WO96/40282 to *Quay et al.*, U.S. Patent 6,231,513 to *Daum et al.* and/or European Patent Application Publication 0135822A2 to *Engel*.

Applicants respectfully believe that such a conclusion is incorrect even before consideration of the amendments herein. Nevertheless, Applicants have amended the claims to make sure the invention will be protected in the appropriate breadth, assuming allowance of the application is forthcoming.

Simply put, Applicants submit that the combination of the *Rössling et al.* and *Uber, III et al.* patents does not render obvious the subject matter recited in independent claims 1 or 140. If one were to combine those two references, all they would yield would be a bubble contrast medium formed by adding water to the pre-packaged (dried, spherically-shaped, gas-containing) microparticles of *Rössling et al.* to rehydrate same and a syringe filled with that bubble contrast medium placed into the system of *Uber, III et al.* After the syringe containing the reconstituted/rehydrated bubble medium is loaded into the system of *Uber et al.*, the combination would result in the same system as that taught in the *Uber, III et al.* patent itself, specifically, a system that is only capable of **reducing** the concentration of bubbles in the medium to a desired level.

Significant here is that, either alone or in combination with the *Rössling et al.* patent, the *Uber, III et al.* system is incapable of increasing the concentration of bubbles to a higher level on the fly should the need to do so arise. Because the *Uber, III et al.* system only discloses **destruction of microbubbles**, the combination of *Rössling et al.* and *Uber, III et al.* fails to teach **real time creation of microbubbles**. Consequently, as bubbles are lost (e.g., by floating/rising in the syringe, reabsorbing into the water, coalescing, etc.), the *Rössling et al./Uber, III et al.* system has no means to maintain the initial high concentration of bubbles in the medium. In contrast, the system of the present claims goes beyond that of the prior art in that it permits real-time creation (and adjustment) of bubbles within a medium in combination with real time administration into the patient. This is something that the combination of the *Rössling et al.* and *Uber, III et al.*, or any of the other prior at, simply does not do.

More specifically, claim 1, as amended, is directed to "*a system for real time creation ... of bubbles for incorporation within a medium to be administered real time into a patient in connection with a medical procedure....*" In addition to a "*bubble generator for creating in real time bubbles of gas within the liquid to form the medium...,*" the claim recites a "*a controller* [that has] *a user interface for enabling an operator to adjust in real time at least one operating parameter of said system pertaining to generation and/or delivery into the patient of the medium inclusive of properties of the bubbles therein for the purpose of at least one of stabilizing and optimizing the medical procedure being performed on the patient.*" These amendments make it clear that the bubbles are created in real time and that the resulting medium is generated for real time administration into the patient so as to optimize according to the demands of the operator a medical procedure being performed on the patient.

The prior art cited in the *Final Office Action* neither individually nor collectively teach or even suggest such a system. More specifically, the systems and apparatuses of the prior art are in no way directed to a system whose bubble generator is capable of creating the bubbles in real time and whose

controller is capable of adjusting in real time at least one operating parameter of the system pertaining to generation and/or delivery into patient of the medium inclusive of the properties of the bubbles in the medium that is being prepared for real time administration into a patient.

Rössling et al. only teach the making of dried microparticles to which water is to be added later for the purpose of re-hydrating to create a bubble-based contrast medium. It discloses a method of making dried spherically-shaped microparticles in which a gas (e.g., air) is enclosed. (col. 2, lines 1-2; col. 9, line 65) The last step of the method involves removing the dried microparticles from column 19, as shown in Figure 1. (col. 5, lines 28-33; col. 10, lines 32-36) Even before this step in the process, the properties of the gas-filled microparticles have become unalterable. (col. 5, lines 28-33) Properties such as the size of the microparticles, the type of gas enclosed in the microparticles, the composition of the shell of the microparticles, etc, are set and cannot be changed on the fly. The dried micro-particulate product is destined only for packaging and shipment for later use at sites where ultrasound imaging procedures can be performed. Once delivered to a site, the dried particles can then be suspended in a pharmaceutically acceptable suspension medium (e.g., water) to create the contrast agent. (col. 3, lines 60-67) Unlike Applicants' claims, the *Rössling et al.* patent thus does not disclose a system whose controller enables an operator to "*adjust in real time* [the] *parameter*[s] ... *pertaining to generation and/or delivery into the patient of the medium inclusive of the properties of the bubbles therein*" for the purpose stabilizing and/or optimizing a medical (e.g., imaging) procedure being performed on the patient.

The *Uber, III et al.* patent discloses a system for producing a contrast-enhanced image of a patient. The system 10 includes a source/syringe 40 of a microbubble contrast medium 30, a pressurizing unit 120 for pressurizing the medium for injection into the patient 20, and an imaging unit 100 for imaging a region of the patient through which the medium will flow. The imaging unit 100

provides an image of that region based upon a signal resulting from the energy that it has applied to the region during the imaging procedure.

Significant here is that system 10 also includes a control unit 92/90, a concentration regulator 60 and a concentration sensor 70. (See e.g., Fig.1; col. 8, lines 56-65; col. 9, lines 17-43) As the medium flows from the syringe 40, it passes through concentration regulator 60 and concentration sensor 70 into patient 20 via fluid path 50 and patient interface 80. Located near the patient, concentration sensor 70 measures the concentration of bubbles in the medium. (col. 9, lines 13-15; col. 10, lines 1-4) The output from sensor 70 and feedback from imaging unit 100 are passed to control unit 92/90 (col. 9, lines 18-25; col. 8, lines 46-48), and control unit 92/90 based on that input (and others) controls the concentration regulator 60. (col. 9, lines 39-43) Specifically, when so commanded by control unit 92/90, the concentration regulator 60 "**destroy[s]** microbubbles 30 ..., for example, by insonating the fluid with ultrasound energy, generating local temperature or pressure changes in the media or by some types of mechanical agitation." (col. 8, lines 58-67)(emphasis added)

Laying out the rationale for bubble destruction, the *Uber, III et al.* patent states that the "ability to **destroy** microbubbles 30 in the fluid path may enable better control of the imaging procedure." (col. 9, lines 1-11)(emphasis added) It then sets forth further detail on microbubble structure and properties and how such knowledge can be employed to devise mechanisms to selectively destroy microbubbles:

> * * * Because mechanical resonance of a bubble wall is a function of bubble size, for example, it may be possible with the proper power and frequency settings to **selectively decrease the concentration of bubbles** of a certain size. Such **selective destruction** allows control of the bubble distribution. Microbubbles 30 can also be **destroyed** in the fluid path as part of a strategy to control contrast agent concentration. It is also possible to reduce the amount of contrast enhancing agent flowing into the patient simply by reducing the flow rate of the media. Id. (emphasis added)

The bottom line is that nowhere in the *Rŏssling et al.* and *Uber, III et al.* patents is the real time creation of bubbles taught or even suggested. Specifically, a system for real time creation of bubbles, of the type recited in claims 1 and 140 wherein a bubble generator permits real time creation of

bubbles within a medium to be administered real time into a patient, is simply not what is covered in the prior art of record.

For the above reasons, Applicants respectfully submit that combined teachings of *Rõssling et al.* and *Uber III et al.* do not render obvious the subject matter recited in independent claims 1 and 140 and their respective dependents. In view of the foregoing amendments and arguments, Applicants believe that the §103(a) rejections have been overcome.

Applicants respectively advise the Examiner that they would welcome an interview to discuss the merits of the claimed invention should the Examiner believe it would prove helpful to advance the present application to allowance.

Lastly, although various claims have been amended or canceled during prosecution, Applicants wish to point out that such revisions are not meant to be construed as an admission of unpatentability of the subject matter recited in earlier versions of the claims. Instead, such revisions should be considered as having been made only to expedite prosecution of the application. They should not be considered as a surrender of the right to pursue any subject matter disclosed in the present application or in any continuation or divisional application based thereon that may be filed in the future.

CONCLUSION

Applicants submit this *Amendment And Response* as part of a *Request for Continued Examination* (RCE). Before entry of this *Amendment And Response*, the present application had forty-three (43) claims pending, two (2) of which independent. Upon entry of this *Amendment And Response*, the number of claims remains unchanged though several have been amended. Earlier in prosecution, ninety eight (98) claims were withdrawn with traverse due to a *Restriction Requirement*.

Given the foregoing amendments and arguments, Applicants respectfully request withdrawal of the rejections set forth in the *Final Office Action* dated 9 December 2009. Applicants believe the application is ready to be allowed. If the Examiner has any questions regarding this *Amendment and Response*, she is invited to call the undersigned at the telephone number listed below.

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